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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,044	04/02/2004	Young Hoon Park	A36218	3943

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EXAMINER	
ARCHIE, NINA	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/817,044	PARK ET AL	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9 and 13-24* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 14-22* is/are withdrawn from consideration.

5)☐ Claim(s) *23* is/are allowed.

6)☐ Claim(s) *1-4 and 24* is/are rejected.

7)☐ Claim(s) *5, 9, 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 3/14/2007. Claims 1, 9 and 24 have been amended. Claims 8 and 10-12 have been cancelled. Claims 1-5, 9, 13 and 23-24 are under examination.

Claim Objections/Rejections Withdrawn

2. In view of the Applicant's amendment and remark the following objections/rejections are withdrawn.

a) Objection to the specification in paragraph [0008] on page 4 is withdrawn in light of applicant's amendment to the specification.
b) Objection to claim 13 is withdrawn in light of light of applicant's amendment.
c) Rejection of claim 1 under 35 U.S.C. 101 is withdrawn in light applicant's amendment thereto.
d) Rejection of claims 8-12 under 35 U.S.C. 112, second paragraph, page 4 paragraphs 1-2 is withdrawn in light of cancellation of claim 8 and in light of applicant's amendment thereto.
e) Rejection of claims 5, 13, and 23 under 35 U.S.C. 112, first paragraph, page paragraphs 1-3 and page 5 paragraph 1 is withdrawn in light of applicant's amendment thereto.
f) Rejection of claims 9-13 under 35 U.S.C. 112, second paragraph, page 5 paragraph 2 is withdrawn in light of applicant's amendment thereto.
g) Rejection of claims 1-4 and 8 under 35 U.S.C. 103 pages 6-7 is withdrawn in light of applicant's amendment thereto.

New Grounds of Rejection

Claim Objections

3. The disclosure is objected to because of the following informalities: Claims 1-3, 5, 9 and 24 recites acronyms "tdcBC", "pckA", and "ppc". While acronyms are permissible shorthand in

the claims, the first recitation should include the full recitation followed by the acronym in parenthesis. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moeckel et al US patent 6,107,063 issued August 22, 2000 in view of Eikmanns et al US patent 6,420,151 issued July 16, 2002, Palmeros et al 2000 Gene 247 255-264, and Debahov et al US patent 4,278,765 issued August 22, 2000.

Claim 1 is drawn to an isolated and purified *Escherichia coli* strain comprising an inactivated chromosomal tdcBC and inactivated pckA genes. At the outset it is noted that Applicants'

specification acknowledges that the threonine dehydratase operon and tdcBC operon are the same as described in the literature (see page 4, paragraph [0009]).

Moeckel et al teaches an *E. coli* strain for the production of threonine. The *E. coli* strain is genetically engineered in that the threonine dehydratase gene (tdcBC operon) of a threonine-producing *Escherichia coli* strain is mutated to deregulate the feedback inhibition of L-isoleucine (see abstract, column 1 lines 5-15). Moeckel et al teach that threonine dehydratase (tdcBC operon) is inactivated by exchanging of one or several bases in the region coding for the allosteric domains of the enzyme and that at least one amino acid in the amino acid sequence of the allosteric domains is replaced by a different one. Moeckel et al teach that threonine dehydratase is mutated in a host cell producing threonine (see column 2 lines).

Moeckel et al does not teach an isolated and purified *Escherichia coli* strain inactivated pckA gene, wherein the pckA gene is inactivated by introducing a foreign pckA gene fragment containing an antibiotic resistance gent having a site-specific recombinase binding site at each of both ends thereof into a parent *Escherichia coli* strain containing an L-threonine degradation-associated operon, tdcBC, that is inactivated, and then allowing homologous recombination between the foreign pckA gene fragment and the pckA gene on chromosome to inactivate the chromosomal pckA gene, wherein the pckA gene is inactivated by removal of the antibiotic resistance gene incorporated there into by the activity of the site-specific recombinas expressed in the Escherichia coli strain and the presence of one copy of the binding site of the site-specific recombinase in the chromosomal pckA gene, wherein the site-specific recombinase is FLP, Cre or XerC/D.

Eickmanns et al US patent 6,420,151 teaches a threonine producing *E. coli* strain that has an attenuated pckA gene. Eickmanns et al teach that the attenuation of the pck gene is advantageous, for the production of L-amino acids, in particular threonine, to eliminate undesirable side reactions. Eickmanns et al teach the mutant pck gene is introduced into a threonine producing *Escherichia coli* strain. Therefore, the DNA fragments coding for the mutant pck gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a pck gene as a wild type enzyme (see abstract, column 2 lines 1-40, columns 3-4, column 6 lines. 60-65, and Examples 1 and 7-8).

Palmeros et al teaches generally inserting a cassette with the DNA fragment into a cleavage site. Palmeros et al teaches a DNA fragment with loxp sites and antibiotic resistance gene having site-specific recombinase such as Cre is inserted into the genome of the *Escherichia coli* strain to allow homologous recombination between the DNA gene fragment and the gene on the chromosome to elute recombinant strains having the deactivated mutant gene (see "Material and Methods").

Debabov et al teach a method for constructing strains that possess an increased capability of producing the required amino acid (i.e. threonine), which produce amino acids by genetic engineering techniques (see Examples).

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to inactivate the chromosomal tdcBC operon of the *E. coli* strain (threonine dehydratase gene) as taught by Moeckel et al and to inactivate the pckA gene of the E. coli strain as taught by Eickmanns et al because both teach E. coli strains to produce L-threonine. It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to introduce a DNA fragment (i.e. pck A gene) into the genome of the *Escherichia coli* strain to allow homologous recombination because Palmeros et al teaches that the system of inserting a DNA fragment into the genome of the *Escherichia coli* strain to allow homologous recombination is useful because no antibiotic resistance markers stay behind on the *Escherichia coli* chromosome and therefore the cell does not carry an antibiotic resistance gene that subsequently would prevent the selection for plasmids or other chromosomal modifications that would depend on such markers and Debabov et al teach having a recipient strain having the mutation blocking the synthesis of the selected amino acid (i.e. threonine) in this strain and the mutation partly blocking the related step of metabolism of the selected amino acid (i.e. threonine) can yield the strain capable of increased productivity of the selected amino acid (i.e. threonine).

5. Claim 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moeckel et al US patent 6,107,063 issued August 22, 2000 in view of Eikmanns et al US patent 6,420,151 issued July 16, 2002, Palmeros et al 2000 Gene 247 255-264, and Debahov et al US patent 4,278,765 issued August 22, 2000.

Claim 24 is drawn to an isolated or purified L-threonine producing strain of *Escherichia coli* wherein the chromosomal tdcBC operon and the chromosomal pckA gene have been inactivated. At the outset it is noted that Applicants' specification acknowledges that the threonine dehydratase operon and tdcBC operon are the same as described in the literature (see page 4, paragraph [0009]).

Moeckel et al teaches an *E. coli* strain for the production of threonine. The *E. coli* strain is genetically engineered in that the threonine dehydratase gene (tdcBC operon) of a threonine-producing *Escherichia coli* strain is mutated to deregulate the feedback inhibition of L-isoleucine (see abstract, column 1 lines 5-15). Moeckel et al teach that threonine dehydratase (tdcBC operon) is inactivated by exchanging of one or several bases in the region coding for the allosteric domains of the enzyme and that at least one amino acid in the amino acid sequence of the allosteric domains is replaced by a different one. Moeckel et al teach that threonine dehydratase is mutated in a host cell producing threonine (see column 2 lines).

Eickmanns et al US patent 6,420,151 teaches a threonine producing *E. coli* strain that has an attenuated pckA gene. Eickmanns et al teach that the attenuation of the pck gene is advantageous, for the production of L-amino acids, in particular threonine, to eliminate undesirable side reactions. Eickmanns et al teach the mutant pck gene is introduced into a threonine producing *Escherichia coli* strain. Therefore, the DNA fragments coding for the mutant pck gene in *Escherichia coli* can be obtained by recombinant DNA by introducing amino acid replacement, insertion, or deletion into a pck gene as a wild type enzyme (see abstract, column 2 lines 1-40, columns 3-4, column 6 lines. 60-65, and Examples 1 and 7-8).

Palmeros et al teaches generally inserting a cassette with the DNA fragment into a cleavage site. Palmeros et al teaches a DNA fragment with loxp sites and antibiotic resistance gene having site-specific recombinase such as Cre is inserted into the genome of the *Escherichia coli* strain to allow homologous recombination between the DNA gene fragment and the gene on the chromosome to elute recombinant strains having the deactivated mutant gene (see "Material and Methods").

Debabov et al teach a method for constructing strains that possess an increased capability of producing the required amino acid (i.e. threonine), which produce amino acids by genetic engineering techniques (see Examples).

It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to inactivate the chromosomal tdcBC operon of the *E. coli* strain (threonine dehydratase gene) as taught by Moeckel et al and to inactivate the chromosomal pckA gene of the E. coli strain as taught by Eickmanns et al because both teach E. coli strains to produce L-threonine. It would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to introduce a DNA fragment (i.e. pck A gene) into the genome of the *Escherichia coli* strain to allow homologous recombination because Palmeros et al teaches that the system of inserting a DNA fragment into the genome of the *Escherichia coli* strain to allow homologous recombination is useful because no antibiotic resistance markers stay behind on the *Escherichia coli* chromosome and therefore the cell does not carry an antibiotic resistance gene that subsequently would prevent the selection for plasmids or other chromosomal modifications that would depend on such markers and Debabov et al teach having a recipient strain having the mutation blocking the synthesis of the selected amino acid (i.e. threonine) in this strain and the mutation partly blocking the related step of metabolism of the selected amino acid (i.e. threonine) can yield the strain capable of increased productivity of the selected amino acid (i.e. threonine).

Citation of Relevant Art

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ozaki et al. Agric. Biol. Chem. 47 No. 7 (1983) 1569-1576 teaches factors that cause an increase in lysine production using various mutants.

Status of the Claims

7. No claims are allowed.

Claims 1-4 and 24 are rejected.

Claims 5, 9 are objected.

Claims 13 are objected as being dependent from a rejected claim.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER